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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS	3	Feb 06	Engineering Information Encompass files have new names
NEWS	4	Feb 16	TOXLINE no longer being updated
NEWS	5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS	6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS	7	May 07	DGENE Reload
NEWS	8	Jun 20	Published patent applications (A1) are now in USPATFULL

NEWS EXPRESS	May 23 CURRENT WINDOWS VERSION IS V6.0a, CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP), AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 17:00:50 ON 21 JUN 2001

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'REGISTRY' ENTERED AT 17:00:56 ON 21 JUN 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 20 JUN 2001 HIGHEST RN 342773-47-1
DICTIONARY FILE UPDATES: 20 JUN 2001 HIGHEST RN 342773-47-1

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

conducting SmartSELECT searches.

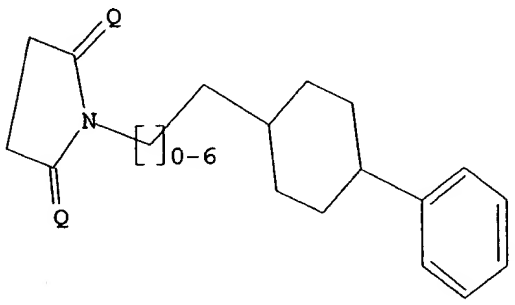
Structure search limits have been increased. See HELP SLIMIT for details.

=>
Uploading 577789b.str

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam

SAMPLE SEARCH INITIATED 17:01:21 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2553 TO ITERATE

39.2% PROCESSED 1000 ITERATIONS 2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 48031 TO 54089
PROJECTED ANSWERS: 2 TO 237

L2 2 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 17:01:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 49000 TO ITERATE

100.0% PROCESSED 49000 ITERATIONS 120 ANSWERS
SEARCH TIME: 00.00.05

L3 120 SEA SSS FUL L1

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	133.56	133.71

FILE 'CAPLUS' ENTERED AT 17:01:40 ON 21 JUN 2001

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1947 - 21 Jun 2001 VOL 134 ISS 26
FILE LAST UPDATED: 20 Jun 2001 (20010620/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

CAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

The CA Lexicon is now available in the Controlled Term (/CT) field. Enter HELP LEXICON for full details.


```
=> s l3 full

L4          56 L3

=> s l4 and hyperplasia?

         16996 HYPERPLASIA?
L5           0 L4 AND HYPERPLASIA?

=> s l4 and prosta?

         97545 PROSTA?
L6           0 L4 AND PROSTA?

=> s l4 and prostatic?

         10559 PROSTATIC?
L7           0 L4 AND PROSTATIC?

=> s l4 and pharmaceutical?

        191412 PHARMACEUTICAL?
L8          14 L4 AND PHARMACEUTICAL?

=> d l8 1-14 ibib abs hitstr


L8   ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        2001:10087  CAPLUS
DOCUMENT NUMBER:         134:66173
TITLE:                   Fluorine-substituted biphenyl butyric acids and their
```

metalloproteinases

INVENTOR(S): Purchase, Claude Forsey, Jr.; Roth, Bruce David; Schielke, Gerald Paul; Walker, Lary Craswell; White, Andrew David

PATENT ASSIGNEE(S): Warner-Lambert, USA

SOURCE: U.S., 31 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

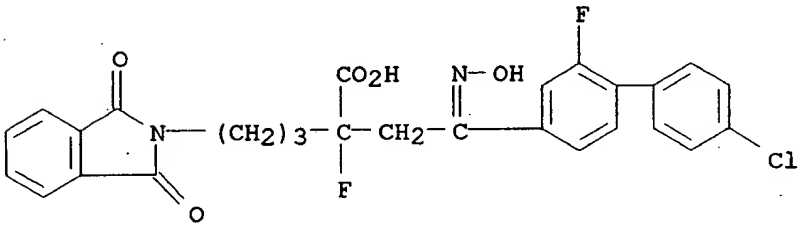
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6169103	B1	20010102	US 1999-256714	19990224

PRIORITY APPLN. INFO.: US 1998-76633 P 19980303
OTHER SOURCE(S): MARPAT 134:66173

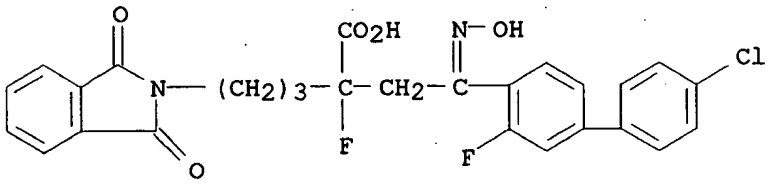
AB Fluorine-substituted biphenyl butyric acid compds. and derivs. are described as well as acid methods for the prepn. and **pharmaceutical** compns. of same, which are useful as inhibitors of matrix metalloproteinases, particularly gelatinase A, stromelysin-1, and collagenase-3, and for the treatment of atherosclerotic plaque rupture, aortic aneurism, heart failure, restenosis, periodontal disease, corneal ulceration, treatment of burns, decubital ulcers, wound healing, cancer, inflammation, pain, arthritis, osteoporosis, multiple sclerosis, renal disease, and other autoimmune or inflammatory disorders dependent upon tissue invasion by leukocytes or other activated migrating cells, acute and chronic neurodegenerative disorders including stroke, head trauma, spinal cord injury, Alzheimer's disease, amyotrophic lateral sclerosis, cerebral amyloid angiopathy, AIDS, Parkinson's disease, Huntington's disease, prion diseases, myasthenia gravis, and Duchenne's muscular dystrophy.

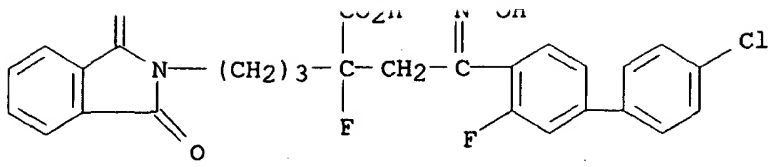
IT **315668-99-6 315669-00-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluorinated butyric acid derivs. as matrix metalloproteinase inhibitors)

RN 315668-99-6 CAPLUS
CN 2H-Isoindole-2-pentanoic acid, .alpha.-[2-(4'-chloro-2-fluoro[1,1'-biphenyl]-4-yl)-2-(hydroxyimino)ethyl]-.alpha.-fluoro-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 315669-00-2 CAPLUS
CN 2H-Isoindole-2-pentanoic acid, .alpha.-[2-(4'-chloro-3-fluoro[1,1'-biphenyl]-4-yl)-2-(hydroxyimino)ethyl]-.alpha.-fluoro-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)





REFERENCE COUNT: 16
REFERENCE(S): (1) Aisen, P; Dementia 1995, V9, P173 CAPLUS
(2) Andersen, K; Neurology 1995, V45, P1441 CAPLUS
(5) Anon; WO 9809940 1998 CAPLUS
(6) Armstrong, P; Can J Cardiol 1994, V10, P214 CAPLUS
(8) Bendeck, M; Circulation Research 1994, V75, P539 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:84604 CAPLUS
DOCUMENT NUMBER: 132:141951
TITLE: **Pharmaceutical** compositions containing ACAT and MMP inhibitors for the treatment of atherosclerotic lesions
INVENTOR(S): Bocan, Thomas Michael Andrew
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004892	A2	20000203	WO 1999-US13948	19990618
WO 2000004892	A3	20000518		
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9947017	A1	20000214	AU 1999-47017	19990618
BR 9912296	A	20010417	BR 1999-12296	19990618
EP 1098662	A2	20010516	EP 1999-930483	19990618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001000291	A	20010118	NO 2001-291	20010118

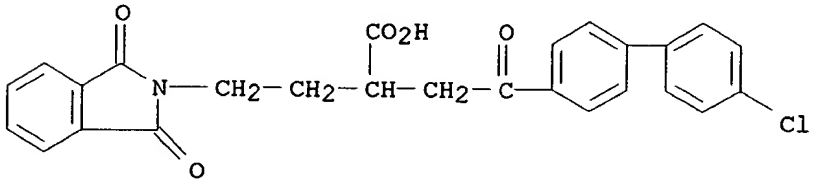
PRIORITY APPLN. INFO.: US 1998-93639 P 19980721
WO 1999-US13948 W 19990618

AB Acyl-CoA:cholesterol acyltransferase (ACAT) and matrix metalloproteinase (MMP) inhibitors are coadministered for the redn. of both the macrophage and smooth muscle cell component of atherosclerotic lesions, thus impairing the expansion of existing lesions and the development of new lesions and for the prevention of plaque rupture and the promotion of lesion regression in a mammal. The direct antiatherosclerotic potential of the combination of ACAT inhibitor, [[2,4,6-tris-(1-methyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl sulfamic acid, and the HMG-CoA reductase inhibitor, simavastatin, in rabbits was studied. A tablet contained 2-(4'-bromobiphenyl-4-sulfonylamino)-3-Me butyric acid
25
ACAT compd. lactose 50, corn starch 20, and magnesium stearate 5 mg.

IT **179546-41-9 179546-43-1**

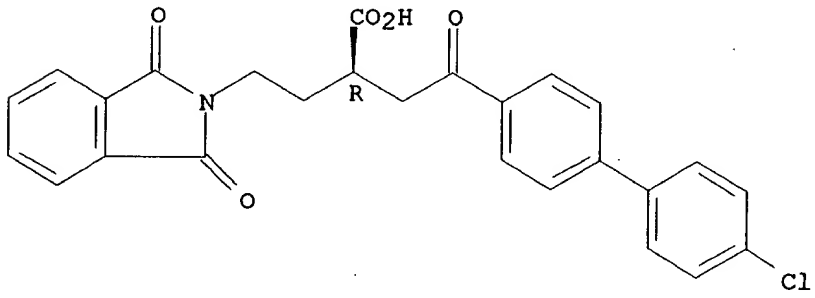
(**pharmaceutical** compns. contg. ACAT and MMP inhibitors for treatment of atherosclerotic lesions)

RN 179546-41-9 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179546-43-1 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (.alpha.R)- (9CI) (CA INDEX NAME)

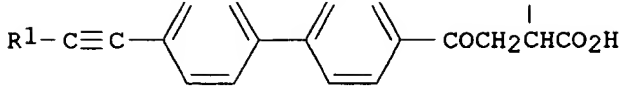
Absolute stereochemistry. Rotation (+).



L8 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:670997 CAPLUS
DOCUMENT NUMBER: 131:283326
TITLE: Matrix metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics
INVENTOR(S): Dixon, Brian R.; Chen, Jinshan
PATENT ASSIGNEE(S): Bayer Corp., USA
SOURCE: U.S., 25 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5968795	A	19991019	US 1997-856694	19970515

PRIORITY APPLN. INFO.: US 1996-645028 P 19960515
US 1996-70454 P 19960515
US 1996-70454 P 19960515
OTHER SOURCE(S): MARPAT 131:283326
GI



I

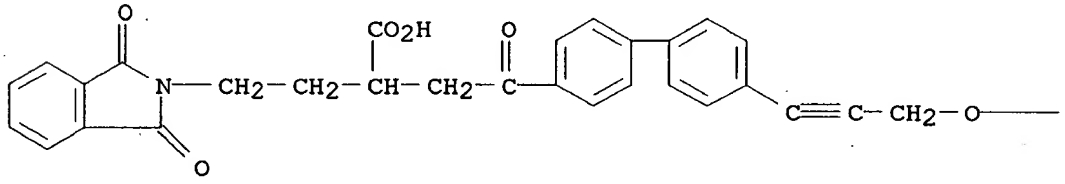
AB Matrix metalloprotease inhibiting compds., **pharmaceutical** compns. thereof and a method of disease treatment using such compds. are presented. The compds. are I (R1=CH2OH, (n-Pr)2NCH2, CH3CO2CH2, EtOCO2CH2, HO(CH2)2, CH3CO2(CH2)2, HO2C(CH2)2, OHC(CH2)3, HO(CH2)4, 3-HO-Ph, PhCH2OCH2; R2=3-phenylpropyl, N-phthalimidoethyl). These compds. are useful for inhibiting matrix metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, rheumatoid arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophic epidermolysis bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, temporomandibular joint disease, demyelinating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic joint injury, and coronary thrombosis from atherosclerotic plaque rupture. The present invention also provides **pharmaceutical** compns. and methods for treating such conditions.

IT **199672-20-3P 199672-21-4P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(matrix metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics)

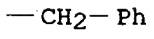
RN 199672-20-3 CAPLUS

CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-1,3-dioxo-.alpha.-[2-oxo-2-[4'-[3-(phenylmethoxy)-1-propynyl][1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

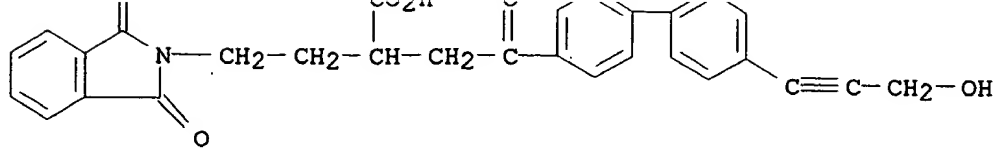


PAGE 1-B

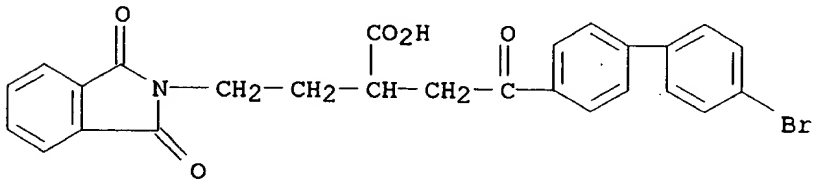


RN 199672-21-4 CAPLUS

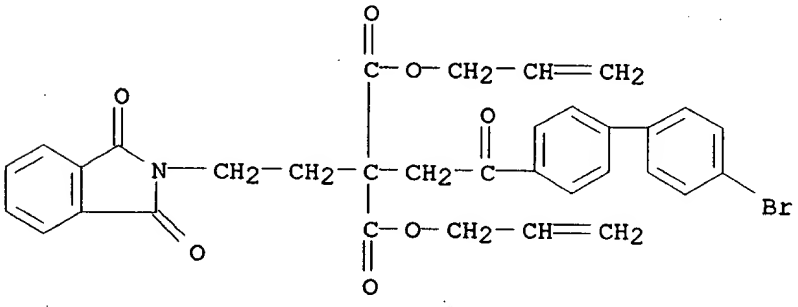
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-.alpha.-[2-[4'-(3-hydroxy-1-propynyl)[1,1'-biphenyl]-4-yl]-2-oxoethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)



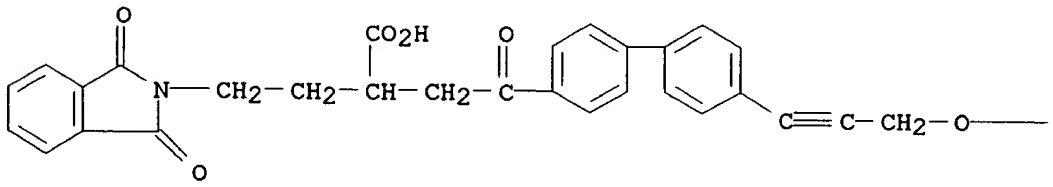
IT **179546-44-2P 199672-27-0P 199672-37-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(matrix metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics)
RN 179546-44-2 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-bromo[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

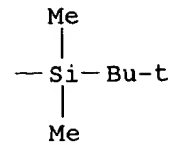


RN 199672-27-0 CAPLUS
CN Propanedioic acid, [2-(4'-bromo[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl]-, di-2-propenyl ester (9CI) (CA
INDEX NAME)



RN 199672-37-2 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-[4'-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-propynyl][1,1'-biphenyl]-4-yl]-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)





REFERENCE COUNT: 8
REFERENCE(S):
(1) Anon; DE 2112716 1972 CAPLUS
(2) Anon; WO 9615096 1996 CAPLUS
(3) Chiccarelli; Arzneim-Forsch 1980, V30(4A), P707 CAPLUS
(4) Child; Arzneim-Forsch 1980, V30(4A), P695 CAPLUS
(5) Child; Journal of Pharmaceutical Sciences 1977, V66(4), P466 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:468334 CAPLUS
DOCUMENT NUMBER: 131:125454
TITLE: Matrix metalloprotease (MMP)-13 selective inhibitors for treatment of arthritis deformans and other MMP-related diseases
INVENTOR(S): McClure, Kim Francis; Lopresti-Morrow, Lori Lynn; Mitchell, Peter Geoffrey; Reeves, Lisa Marie; Reiter, Lawrence Alan; Robinson, Ralph Pelton; Yocum, Sue Ann
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

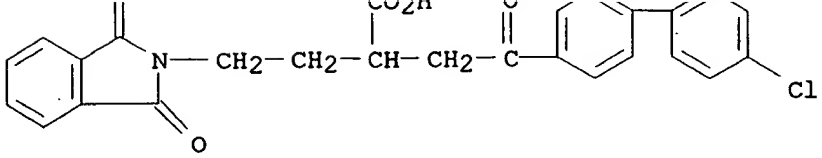
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11199512	A2	19990727	JP 1998-289540	19981012
EP 935963	A2	19990818	EP 1998-308563	19981020
EP 935963	A3	20001004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2251197	AA	19990424	CA 1998-2251197	19981022
AU 9889481	A1	19990520	AU 1998-89481	19981022

PRIORITY APPLN. INFO.: US 1997-62766 P 19971024

AB Matrix metalloprotease (MMP)-13 selective inhibitors including 1-{[4-(4-fluorophenoxy)benzenesulfonyl]-pyridin-3-ylmethylamino}-cyclopentanecarboxylic acid and other compds. and their **pharmaceutically** acceptable salts are claimed for treatment of arthritis deformans and other MMP-related diseases. The inhibitory effects of these compds. on MMP 1 and MP 13 were tested.

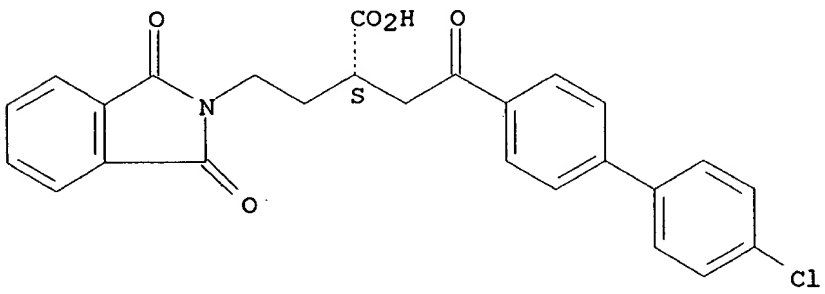
IT **179546-41-9 179546-42-0**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix metalloprotease (MMP)-13 selective inhibitors for treatment of arthritis deformans and other MMP-related diseases)

RN 179546-41-9 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179546-42-0 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:464267 CAPLUS
DOCUMENT NUMBER: 131:116517
TITLE: Preparation of N-acyl-phenylalanine derivatives as inhibitors of .alpha.4-mediated cell adhesion
INVENTOR(S): Sircar, Ila; Gudmundsson, Kristjan S.; Martin, Richard
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 243 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936393	A1	19990722	WO 1999-US993	19990119
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9924584	A1	19990802	AU 1999-24584	19990119
BR 9907040	A	20001017	BR 1999-7040	19990119
EP 1049662	A1	20001108	EP 1999-904115	19990119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-71840 P 19980120
WO 1999-US993 W 19990119
OTHER SOURCE(S): MARPAT 131:116517
GI For diagram(s), see printed CA Issue.
AB The present invention relates to a **pharmaceutical** compn.

Y is a bond, carbonyl, lower alkylene optionally substituted by HO or Ph, lower alkenylene, or -O-(lower alkylene)-; n is 0, 1 or 2; Z is oxygen or sulfur; W is oxygen, sulfur, -CH:CH-, -NH- or -N:CH-; R1, R2 and R3 are the same or different and are hydrogen, halogen, hydroxyl, a substituted or unsubstituted lower alkyl group, a substituted or unsubstituted lower alkoxy group, a substituted or unsubstituted amino group, CO2H or an amide or an ester thereof, cyano, lower alkylthio, lower alkanesulfonyl, substituted or unsubstituted SO2NH2, etc.; R4 is tetrazolyl, carboxyl group, amide or ester; R5 is hydrogen, nitro, amino, hydroxyl, lower alkanoyl, lower alkyl, etc.; R6 is selected from (a) a substituted or unsubstituted Ph group, (b) a substituted or unsubstituted pyridyl group, (c) a substituted or unsubstituted thienyl group, (d) a substituted or unsubstituted benzofuranyl group, etc.; or a **pharmaceutically** acceptable salt thereof]. These phenylalanine derivs. are useful for treating or preventing conditions caused by .alpha.4-mediated cell adhesion such as rheumatoid arthritis, asthma, psoriasis, eczema, contact dermatitis and other skin inflammatory diseases, diabetes, multiple sclerosis, systemic lupus erythematosus (SLE), inflammatory bowel disease including ulcerative colitis and Crohn's disease, and other diseases involving leukocyte infiltration of the gastrointestinal tract, or other epithelial lined tissues, such as skin, urinary tract, respiratory airway, and joint synovium.

N-(tert-butoxycarbonyl)-O-(trifluoromethanesulfonyl)-L-tyrosine Me ester (prepn. given) was coupled with 2-methoxybenzene boronic acid in toluene/DMF in the presence of K2CO3 and Pd(PPh3)4 at 80 .degree.C for 24 h to give N-(tert-butoxycarbonyl)-4-(2-methoxyphenyl)-L-phenylalanine Me ester. The latter compd. was treated with CF3CO2H in CH2Cl2 for 1.5 h to remove the Boc group and then condensed with 2,6-dichlorobenzoyl chloride in the presence of diisopropylethylamine at room temp. for 24 h to give N-(2,6-dichlorobenzoyl)-4-(2-methoxyphenyl)-L-phenylalanine Me ester (II) which was sapond. with LiOH in THF/MeOH at room temp. for 3 h, evapd., treated with H2O, adjusted Ph 2, and extd. with EtOAc to give N-(2,6-dichlorobenzoyl)-4-(2-methoxyphenyl)-L-phenylalanine (III). II and III in vitro inhibited at IC50 of 1.gtoreq. and 0.3.gtoreq. .mu.M, resp., .beta.7-mediated cell adhesion which measured the adhesive interactions of a B-cell line, RPMI, known to express .alpha.4.beta.7, to the alternatively spliced region of fibronectin referred to as CS-1, in the presence of test compds.

IT **232275-27-3P**

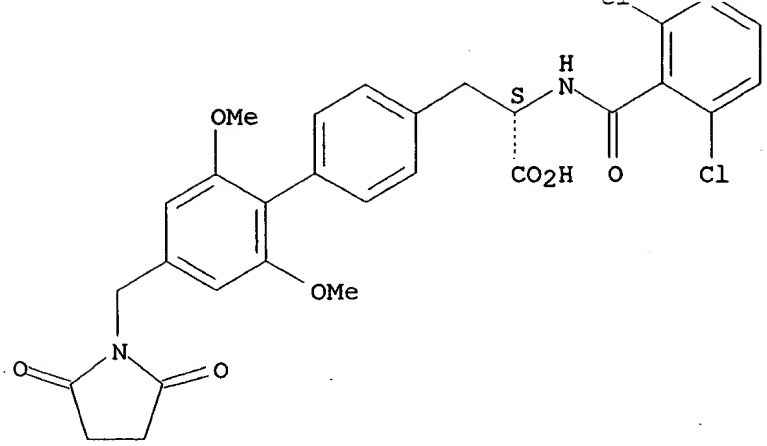
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-acyl-phenylalanine derivs. as inhibitors of .alpha.4-mediated cell adhesion for prevention and treatment of diseases caused by .alpha.4-mediated cell adhesion)

RN 232275-27-3 CAPLUS

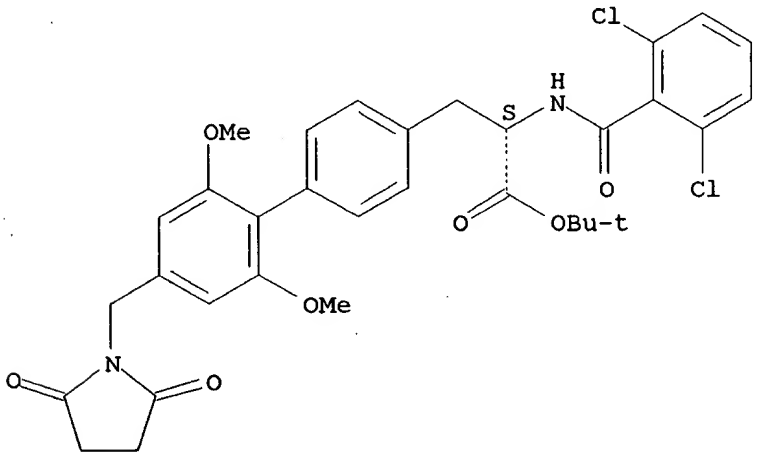
CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[(2,6-dichlorobenzoyl)amino]-4'-[(2,5-dioxo-1-pyrrolidinyl)methyl]-2',6'-dimethoxy-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **232277-11-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-acyl-phenylalanine derivs. as inhibitors of .alpha.4-mediated cell adhesion for prevention and treatment of diseases caused by .alpha.4-mediated cell adhesion)
RN 232277-11-1 CAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[(2,6-dichlorobenzoyl)amino]-4'-[(2,5-dioxo-1-pyrrolidinyl)methyl]-2',6'-dimethoxy-, 1,1-dimethylethyl ester, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



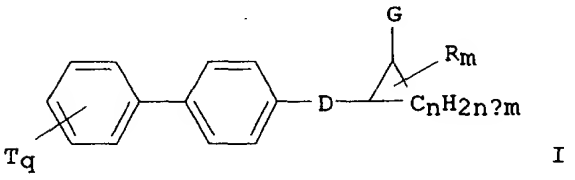
REFERENCE COUNT: 4
REFERENCE(S):
(1) Anon; 1966, 10
(2) Biogen; WO 9622966 A 1996 CAPLUS
(3) Hoffmann-La Roche, F; WO 9910312 A 1999 CAPLUS
(4) Sokolov, S; Zh Organ Khim 1966, V2(6), P1088 CAPLUS

L8 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:205318 CAPLUS
DOCUMENT NUMBER: 130:267212
TITLE: Biphenyl-derived substituted cycloalkanecarboxylic acid derivatives and analogs as matrix metalloprotease inhibitors
INVENTOR(S): Kluender, Harold Clinton Eugene; Bullock, William Harrison; Dixon, Brian Richard; Schneider, Stephan;

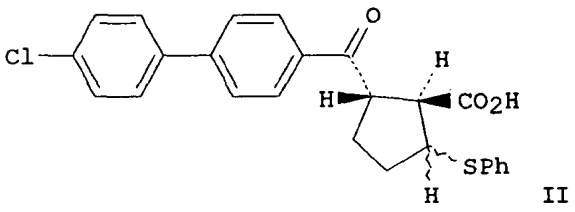
McClelland; Wolanin, Donald John
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S., 102 pp., Cont. of U.S. Ser. No. 463,471, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5886022	A	19990323	US 1997-866568	19970530

PRIORITY APPLN. INFO.: US 1995-463471 19950605
OTHER SOURCE(S): MARPAT 130:267212
GI



I



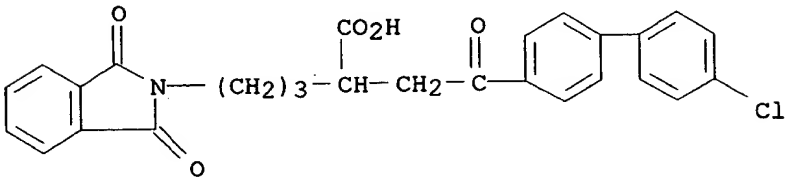
II

AB The invention discloses inhibitors for matrix metalloproteases (MMPs), **pharmaceutical** compns. contg. the inhibitors, and a process for using them to treat a variety of physiol. conditions. The claimed compds. have the generalized formula I [wherein each T = halo, alk(en/yn)yl, (CH2)pQ, etc.; Q = aryl, heteroaryl, cyano, CHO, NO2, etc.; p = 0-4; q = 0-2; D = CO, CH(OH), C:NOH, C:S; n = 2 or 3; R = alk(en/yn)yl, aralk(en/yn)yl; G = CO2H, alkoxycarbonyl, (di)(alkyl)carbamoyl, or amino acid residues bound at N via a CO linker; m = 0-2]. Approx. 250 compds. including both I and many acyclic carboxylic acid analogs were prepd. For instance, Friedel-Crafts acylation of 4-chlorobiphenyl by 1-cyclopentene-1,2-dicarboxylic anhydride, followed by lithiation/reprotonation to effect double-bond isomerization, and Michael addn. of thiophenol to the double bond, gave 2 diastereomers of title compd. II. The trans,trans isomer of II was the most active diastereomer, with IC50 values as follows: MMP-3 14-47 nM, MMP-9 56 nM, and MMP-2 4 nM.

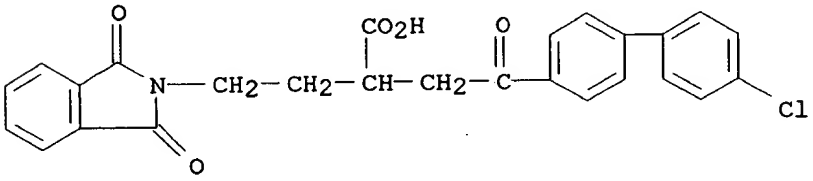
IT **179546-35-1P**, .alpha.-[2-(4'-Chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-pentanoic acid
179546-41-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

RN 179546-35-1 CAPLUS

.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-
2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179546-41-9 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32
REFERENCE(S): (1) Anon; BE 667498 1965 CAPLUS
(3) Anon; GB 1565616 1980 CAPLUS
(4) Anon; DE 2854475 1980 CAPLUS
(5) Anon; FR 2503140 1982 CAPLUS
(6) Anon; JP 60209539 1985 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

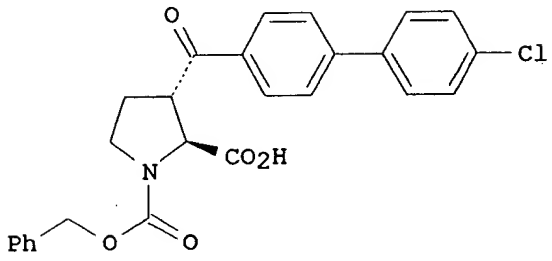
L8 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:534889 CAPLUS
DOCUMENT NUMBER: 129:161412
TITLE: Derivatives of substituted 4-biarylbutyric acid as matrix metalloprotease inhibitors
INVENTOR(S): Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt, Michael Christopher; Wolanin, Donald John; Wilhelm, Scott M.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S., 109 pp. Cont.-in-part of U.S. Ser. No. 339,846.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5789434	A	19980804	US 1995-539409	19951106
CA 2201863	AA	19960523	CA 1995-2201863	19951109
CN 1163604	A	19971029	CN 1995-196209	19951109
HU 78083	A2	19990830	HU 1998-233	19951109
US 5874473	A	19990223	US 1997-864666	19970528
US 5886024	A	19990323	US 1997-865325	19970528
US 5854277	A	19981229	US 1997-865639	19970530
US 5859047	A	19990112	US 1997-866798	19970530

US 5861428	A	19990119	US 1997-866680		19970530
US 5886043	A	19990323	US 1997-866778		19970530
US 6166082	A	20001226	US 1998-57679		19980409
PRIORITY APPLN. INFO.:			US 1994-339846	A2	19941115
			US 1995-462729	B1	19950605
			US 1995-463490	B1	19950605
			US 1995-463580	B1	19950605
			US 1995-463794	B1	19950605
			US 1995-464253	B1	19950605
			US 1995-465626	B1	19950605
			US 1995-539409	A1	19951106

OTHER SOURCE(S): MARPAT 129:161412

GI



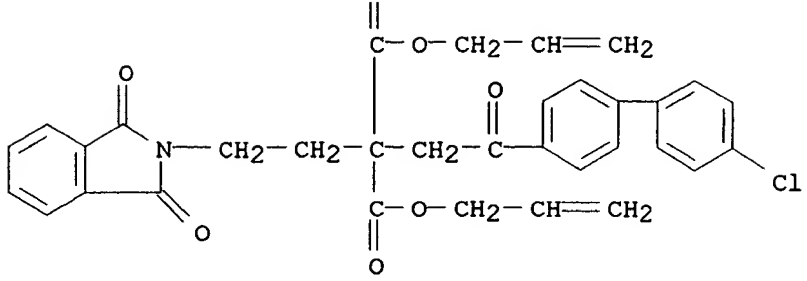
I

AB Matrix metalloprotease (MMP) inhibitors TxA-B-D-E-G [I; T = halo, haloalkyl, alkynyl, (un)substituted alkyl or alkenyl; x = 0, 1, 2; A, B = arom. or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, 5-tetrazolyl, etc.] and their **pharmaceutically** acceptable salts were prepd. In particular, I [A = C6H4; B = 1,4-C6H4; E = certain substituted THF, tetrahydrothiophene, or pyrrolidine divalent radicals] with MMP inhibitory activity, and their **pharmaceutically** acceptable salts, are claimed. For instance, claimed title compd. II was prepd. from L-pyroglutaminol in 9 steps. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. For instance, II had corresponding IC50 values of 103, 381, and 35 nM. I inhibited tumor growth and metastasis in animal models, and inhibited cartilage lesions in a guinea pig model of osteoarthritis.

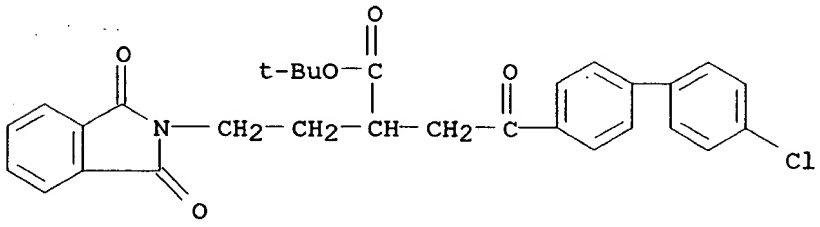
IT **179548-41-5P 179549-09-8P 179549-16-7P 179549-17-8P 179549-18-9P 179549-19-0P 179549-20-3P 188675-85-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179548-41-5 CAPLUS

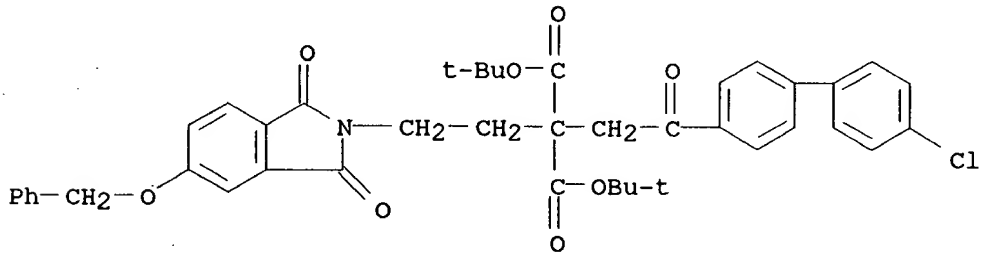
CN Propanedioic acid, [2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl]-, di-2-propenyl ester (9CI) (CA INDEX NAME)



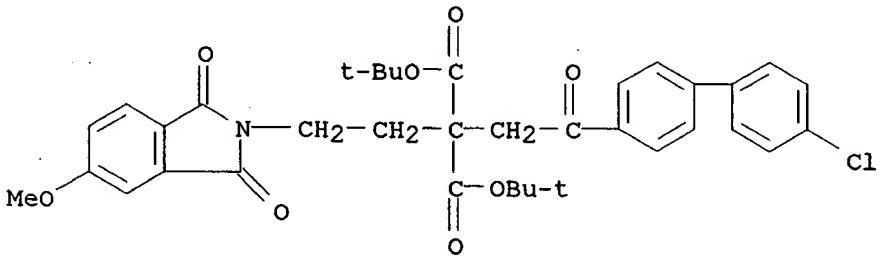
RN 179549-09-8 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



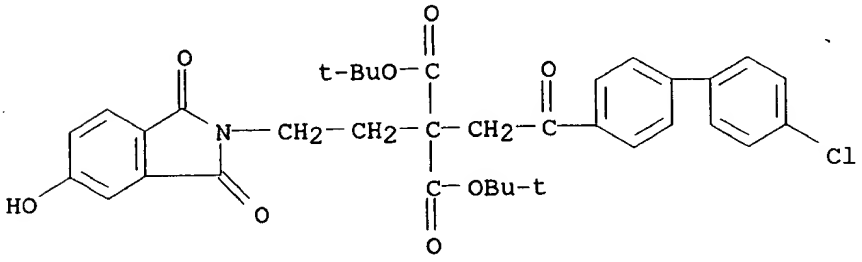
RN 179549-16-7 CAPLUS
CN Propanedioic acid, [2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-[1,3-dihydro-1,3-dioxo-5-(phenylmethoxy)-2H-isoindol-2-yl]ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



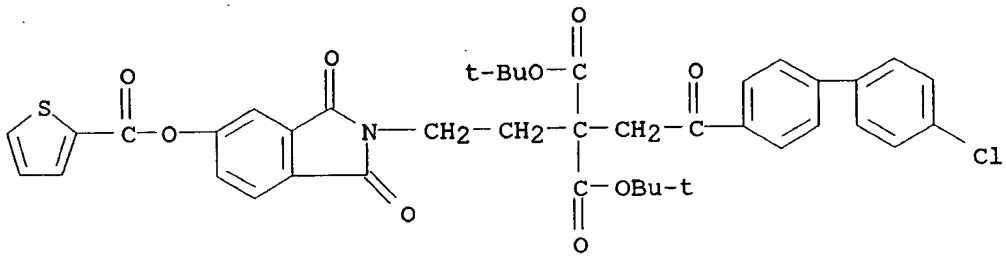
RN 179549-17-8 CAPLUS
CN Propanedioic acid, [2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-(1,3-dihydro-5-methoxy-1,3-dioxo-2H-isoindol-2-yl)ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



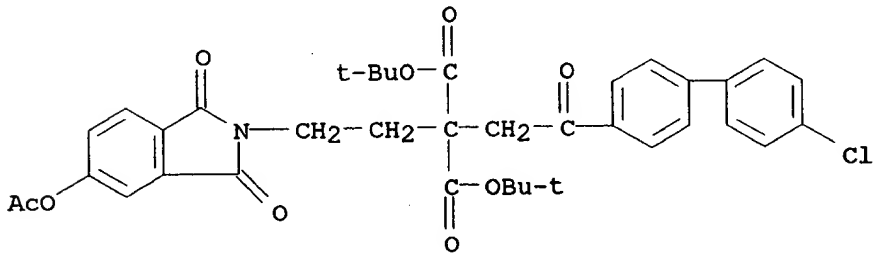
CN Propanedioic acid, [2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-(1,3-dihydro-5-hydroxy-1,3-dioxo-2H-isoindol-2-yl)ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



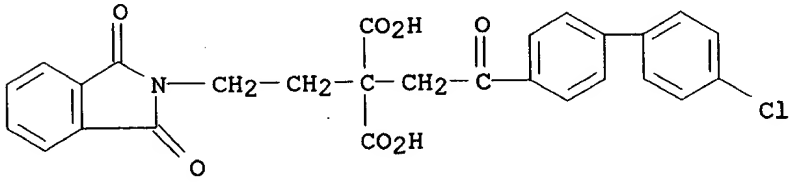
RN 179549-19-0 CAPLUS
CN Propanedioic acid, [2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-[1,3-dihydro-1,3-dioxo-5-[(2-thienylcarbonyl)oxy]-2H-isoindol-2-yl]ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 179549-20-3 CAPLUS
CN Propanedioic acid, [2-[5-(acetyloxy)-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl]ethyl][2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



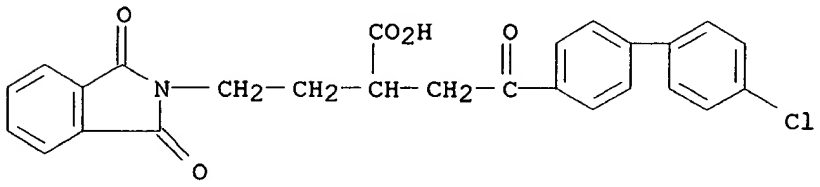
RN 188675-85-6 CAPLUS
CN Propanedioic acid, [2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl]- (9CI) (CA INDEX NAME)



IT **179546-41-9P 179546-42-0P**

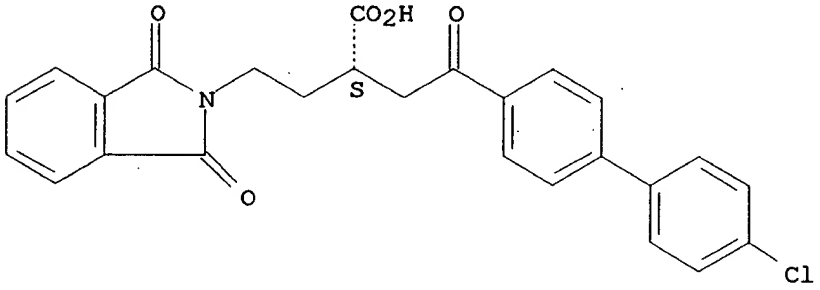
(Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179546-41-9 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179546-42-0 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (.alpha.S)- (9CI) (CA INDEX NAME)

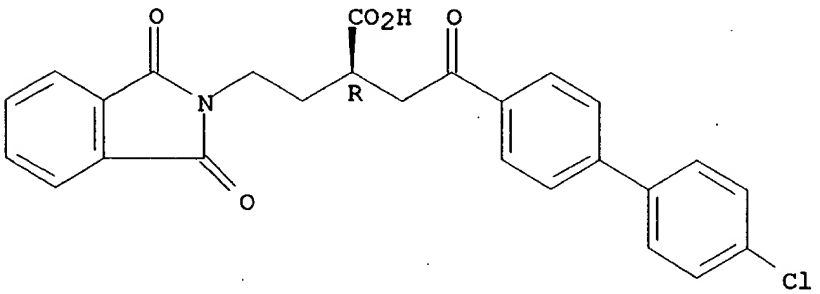
Absolute stereochemistry. Rotation (-).



IT **179546-43-1P**
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179546-43-1 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (.alpha.R)- (9CI) (CA INDEX NAME)

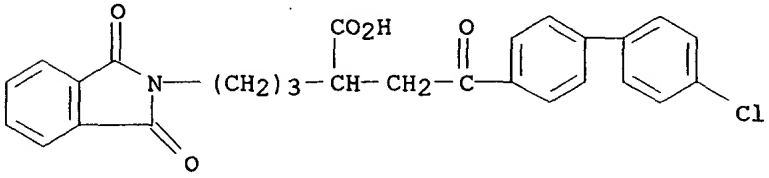
Absolute stereochemistry. Rotation (+).



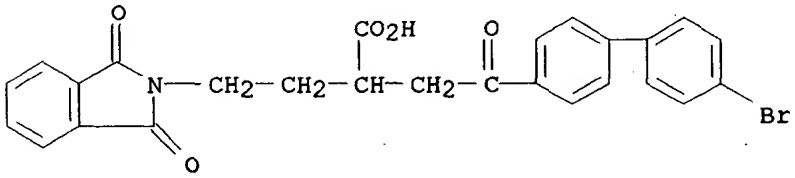
IT **179546-35-1P 179546-44-2P 179546-45-3P**

179547-44-5P 179547-45-6P 179547-46-7P
179547-47-8P 179547-48-9P 179547-50-3P
179547-51-4P 179547-52-5P 179547-53-6P
179547-54-7P 179547-55-8P 179547-56-9P
179547-58-1P 179547-59-2P 179547-60-5P
179547-61-6P 179547-62-7P 179547-63-8P
179547-64-9P 179547-68-3P 179547-70-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

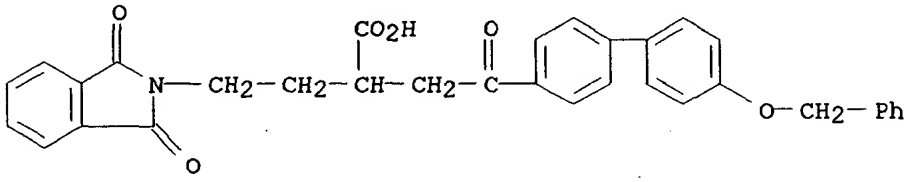
RN 179546-35-1 CAPLUS
CN 2H-Isoindole-2-pentanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



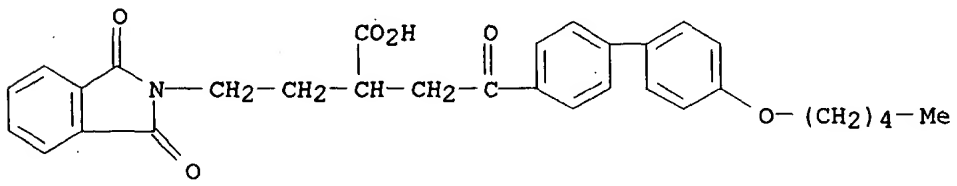
RN 179546-44-2 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-bromo[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

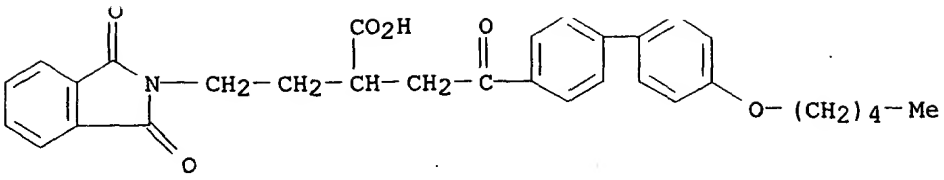


RN 179546-45-3 CAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-1,3-dioxo-.alpha.-[2-oxo-2-[4'-(phenylmethoxy)[1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)

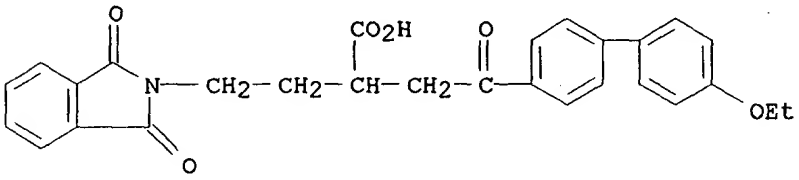


RN 179546-46-4 CAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-1,3-dioxo-.alpha.-[2-oxo-2-[4'-(pentyloxy)[1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)

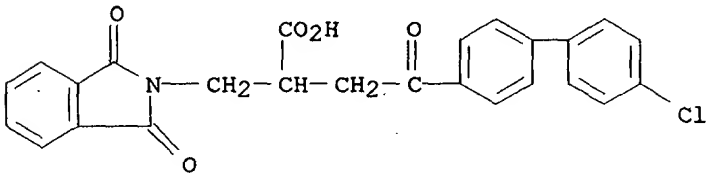




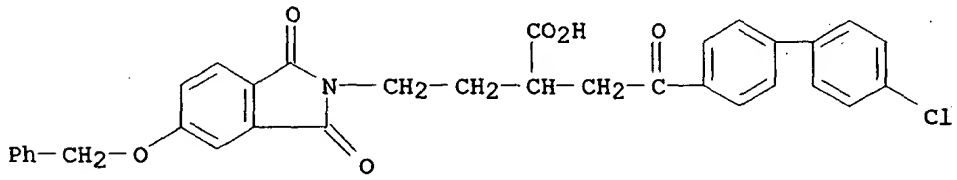
RN 179546-47-5 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



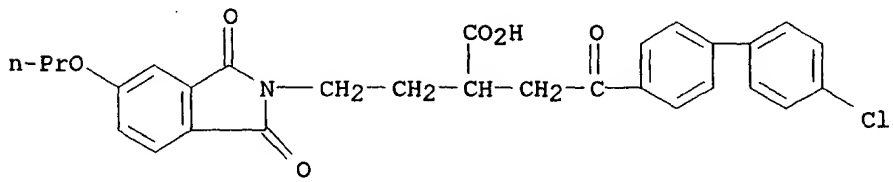
RN 179546-48-6 CAPLUS
CN 2H-Isoindole-2-propanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-
2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179547-44-5 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

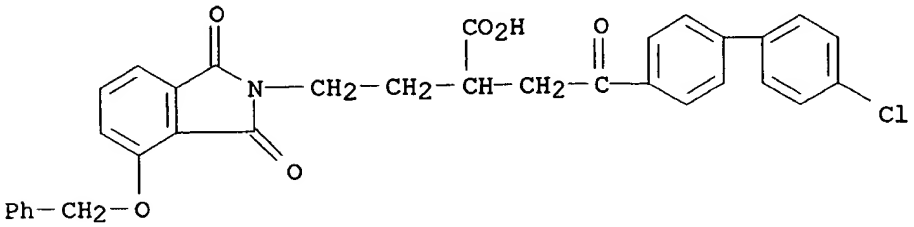


RN 179547-45-6 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo-5-propoxy- (9CI) (CA INDEX NAME)

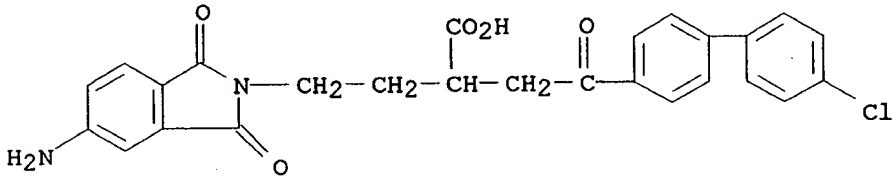


RN 179547-46-7 CAPLUS

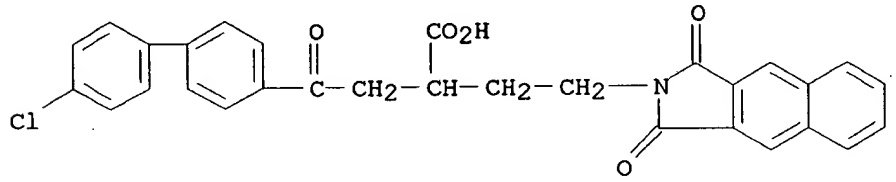
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 179547-47-8 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
5-amino-.alpha.-[2-(4'-chloro[1,1'-biphenyl]-
4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

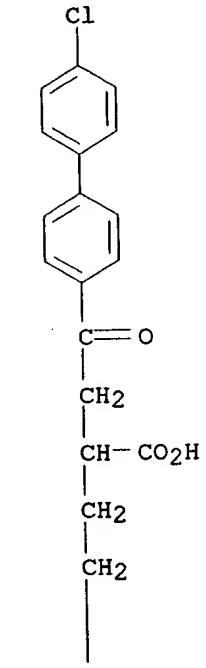


RN 179547-48-9 CAPLUS
CN 2H-Benz[f]isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-
4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

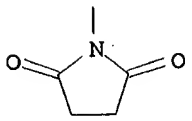


RN 179547-50-3 CAPLUS
CN 1-Pyrrolidinebutanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)

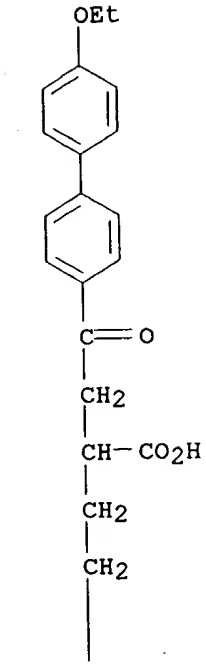
PAGE 1-A

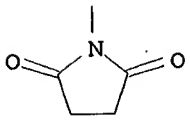


PAGE 2-A

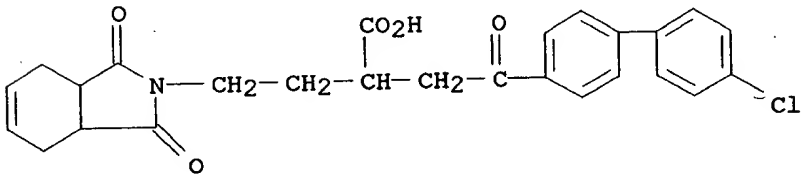


RN 179547-51-4 CAPLUS
CN 1-Pyrrolidinebutanoic acid, .alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)

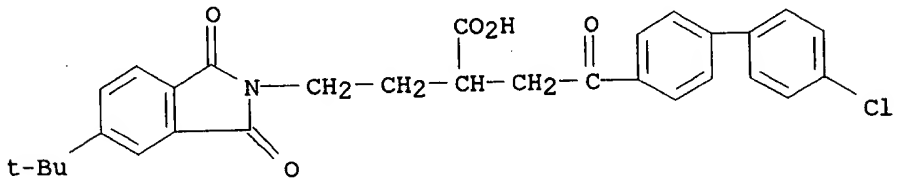




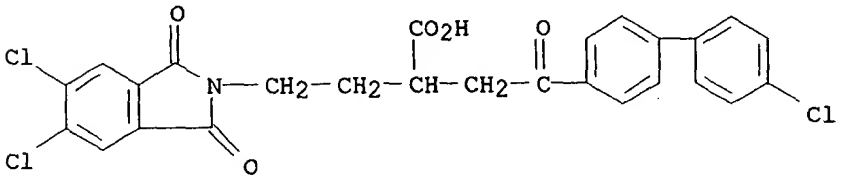
RN 179547-52-5 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3,3a,4,7,7a-hexahydro-1,3-dioxo- (9CI) (CA INDEX NAME)



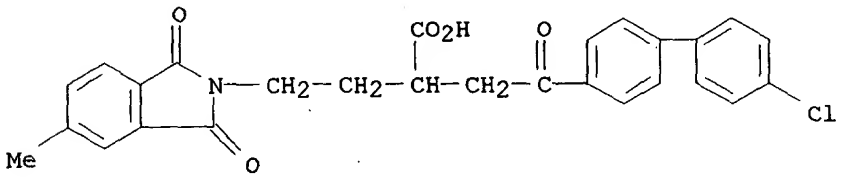
RN 179547-53-6 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-5-(1,1-dimethylethyl)-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



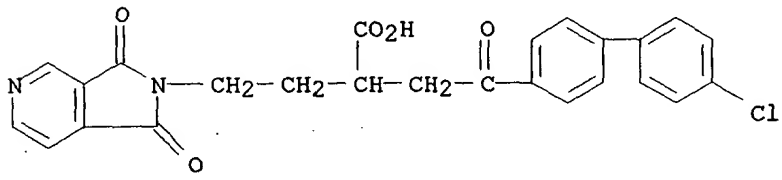
RN [illegible]
CN 2H-Isoindole-2-butanoic acid, 5,6-dichloro-.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



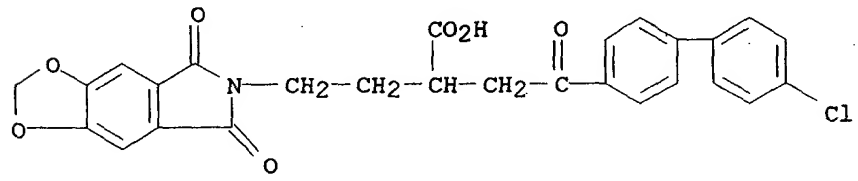
RN 179547-55-8 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-5-methyl-1,3-dioxo- (9CI) (CA INDEX NAME)



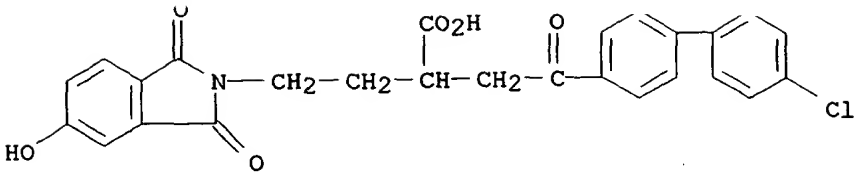
RN 179547-56-9 CAPLUS
CN 2H-Pyrrolo[3,4-c]pyridine-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179547-58-1 CAPLUS
CN 6H-1,3-Dioxolo[4,5-f]isoindole-6-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-5,7-dihydro-5,7-dioxo- (9CI) (CA INDEX NAME)



RN 179547-59-2 CAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-5-hydroxy-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179547-60-5 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-4-hydroxy-1,3-dioxo- (9CI) (CA INDEX NAME)

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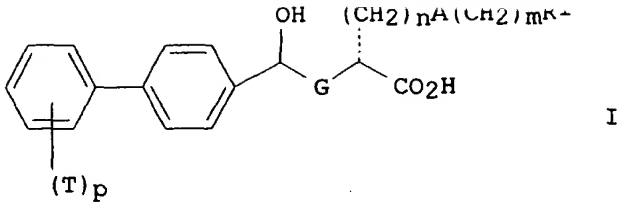
=> d l8 8-14 ibib abs hitstr

L8 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:352815 CAPLUS
DOCUMENT NUMBER: 129:27819
TITLE: Substituted 4-biphenyl-4-hydroxybutyric acid derivatives as matrix metalloprotease inhibitors
INVENTOR(S): Kluender, Harold C. E.; Bjorge, Susan M.; Zadjura, Lisa Marie; Brubaker, William Frederick
PATENT ASSIGNEE(S): Bayer Corp., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822436	A1	19980528	WO 1997-US19960	19971030
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851024	A1	19980610	AU 1998-51024	19971030
AU 731830	B2	20010405		
EP 937036	A1	19990825	EP 1997-945585	19971030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9712707	A	19991026	BR 1997-12707	19971030
CN 1241177	A	20000112	CN 1997-180910	19971030
JP 2001505877	T2	20010508	JP 1998-523677	19971030
NO 9901994	A	19990615	NO 1999-1994	19990427

PRIORITY APPLN. INFO.: US 1996-30264 P 19961031
WO 1997-US19960 W 19971030
OTHER SOURCE(S): MARPAT 129:27819
GI



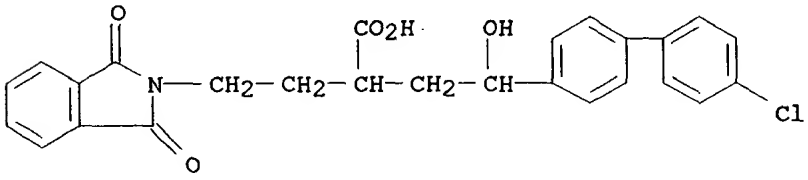
I

AB The title compds. I (T = **pharmaceutically** acceptable substituent group; p = 0-2; m = 0-4; n = 0, 1; A = CH2, CH, N; G = CH2, CH; R1 = substituent group; A and G may be joined), matrix metalloprotease inhibitors, were prepd. E.g., (S)-4-[4-(4-chlorophenyl)phenyl]-4-oxo-2-(phenylthiomethyl)butanoic acid was reduced with NaBH4 to give (2S,4R)- and (2S,4S)-4-[4-(4-chlorophenyl)phenyl]-4-hydroxy-2-(phenylthiomethyl)butanoic acids.

IT **208049-74-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenylhydroxybutyric acid derivs. as matrix metalloprotease inhibitors)

RN 208049-74-5 CAPLUS

CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-hydroxyethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



L8 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:476807 CAPLUS

DOCUMENT NUMBER: 125:142275

TITLE: Substituted 4-biarylbutyric or 5-biarylpentanoic acids and derivatives as matrix metalloprotease inhibitors

INVENTOR(S): Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt, Michael Christopher; et al.

PATENT ASSIGNEE(S): Bayer A.-G., USA

SOURCE: PCT Int. Appl., 263 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615096	A1	19960523	WO 1995-US14002	19951109

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM

IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2201863	AA	19960523	CA 1995-2201863	19951109
AU 9641975	A1	19960606	AU 1996-41975	19951109
AU 702317	B2	19990218		
EP 790974	A1	19970827	EP 1995-940572	19951109

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

BR 9509686	A	19970930	BR 1995-9686	19951109
CN 1163604	A	19971029	CN 1995-196209	19951109
JP 10509146	T2	19980908	JP 1995-516097	19951109
HU 78083	A2	19990830	HU 1998-233	19951109
FI 9702062	A	19970714	FI 1997-2062	19970514
NO 9702220	A	19970714	NO 1997-2220	19970514
US 5874473	A	19990223	US 1997-864666	19970528
US 5886024	A	19990323	US 1997-865325	19970528
US 5854277	A	19981229	US 1997-865639	19970530
US 5859047	A	19990112	US 1997-866798	19970530
US 5861427	A	19990119	US 1997-866679	19970530
US 5861428	A	19990119	US 1997-866680	19970530
US 5886043	A	19990323	US 1997-866778	19970530

PRIORITY APPLN. INFO.:	US 1994-339846	A	19941115
	US 1995-462729	B1	19950605
	US 1995-463490	B1	19950605
	US 1995-463580	B1	19950605
	US 1995-463794	B1	19950605
	US 1995-464253	B1	19950605
	US 1995-465626	B1	19950605
	WO 1995-US14002	W	19951109

OTHER SOURCE(S): MARPAT 125:142275

AB Matrix metalloprotease inhibitors TxA-B-D-E-G [Tx = substituent such as halo, C1-C10 alkyl, or cyanoalkenyl; x = 0, 1, 2; A, B = arom. or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, etc.] and their **pharmaceutically** acceptable salts were prepd. Thus, (S)-.gamma.-oxo-4'-(pentyloxy)-.alpha.-(3-phenylpropyl)-[1,1'-biphenyl]-4-butanoic acid (86) was prepd. via alkylation of di-Et (3-phenylpropyl)malonate with 2,4'-dibromoacetophenone, followed by sapon.-monodecarboxylation, reaction with 4-methoxybenzeneboronic acid, Me ether cleavage, and O-pentylation. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. Using compds. such as 86, the no. of tumor metastases was decreased between 38 and 49% as compared to the control. The title compds. were also assayed for inhibition of cartilage lesions in a guinea pig model of osteoarthritis.

IT **179546-41-9P**

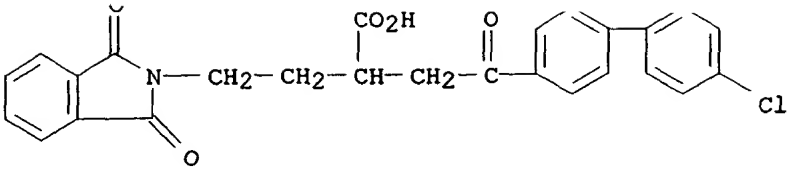
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

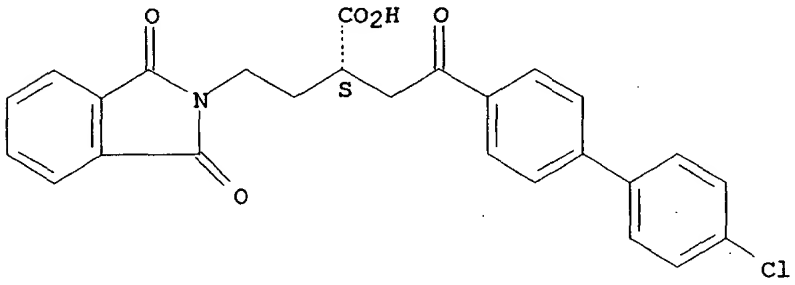
RN 179546-41-9 CAPLUS

CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

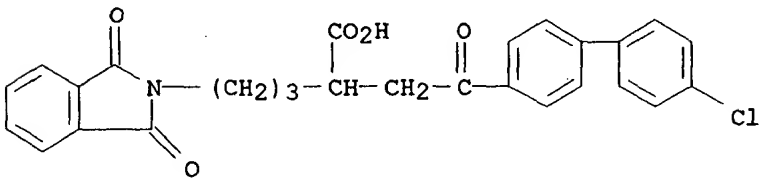


IT **179546-42-0P**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); RCT (Reactant); SPN (Synthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)
RN 179546-42-0 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (.alpha.S)- (9CI) (CA INDEX NAME)

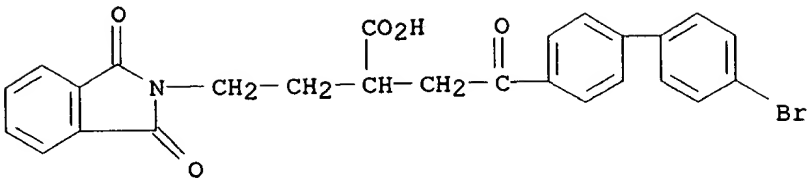
Absolute stereochemistry. Rotation (-).



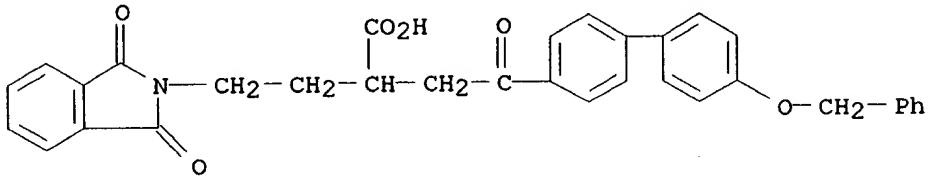
IT **179546-35-1P 179546-44-2P 179546-45-3P**
179546-46-4P 179546-47-5P 179546-48-6P
179547-44-5P 179547-45-6P 179547-46-7P
179547-47-8P 179547-48-9P 179547-50-3P
179547-51-4P 179547-52-5P 179547-53-6P
179547-54-7P 179547-55-8P 179547-56-9P
179547-58-1P 179547-59-2P 179547-60-5P
179547-61-6P 179547-62-7P 179547-63-8P
179547-64-9P 179547-68-3P 179547-70-7P
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)
RN 179546-35-1 CAPLUS
CN 2H-Isoindole-2-pentanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



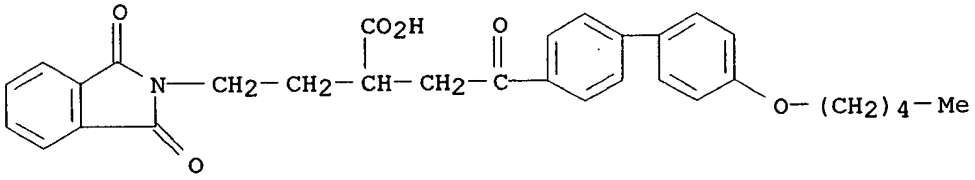
RN 179546-44-2 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-bromo[1,1'-biphenyl]-4-yl)-2-



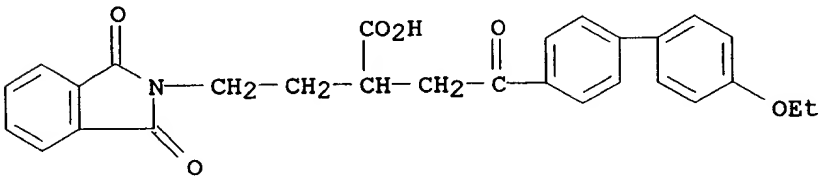
RN 179546-45-3 CAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-1,3-dioxo-.alpha.-[2-oxo-2-[4'-(phenylmethoxy)[1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)



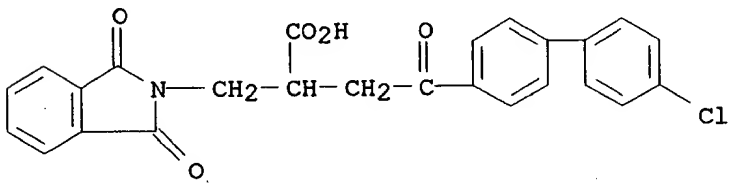
RN 179546-46-4 CAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-1,3-dioxo-.alpha.-[2-oxo-2-[4'-(pentyloxy)[1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)



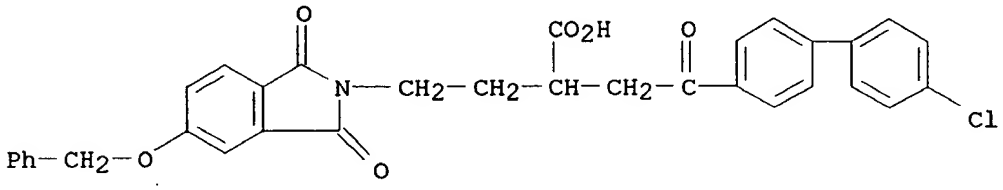
RN 179546-47-5 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



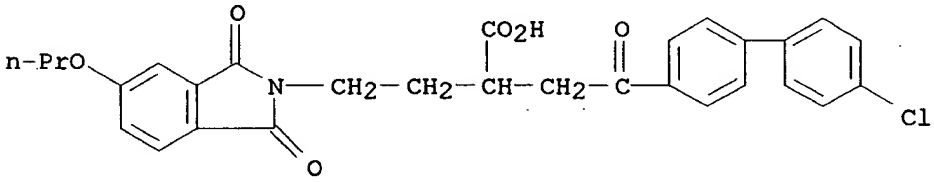
RN 179546-48-6 CAPLUS
CN 2H-Isoindole-2-propanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



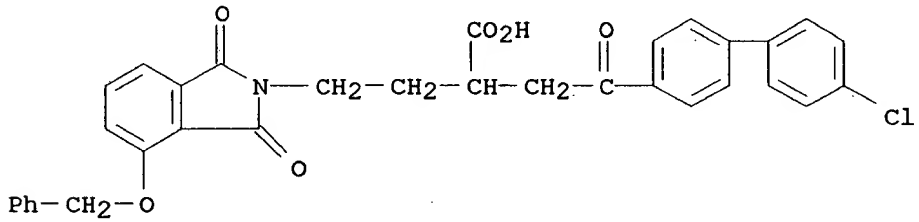
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



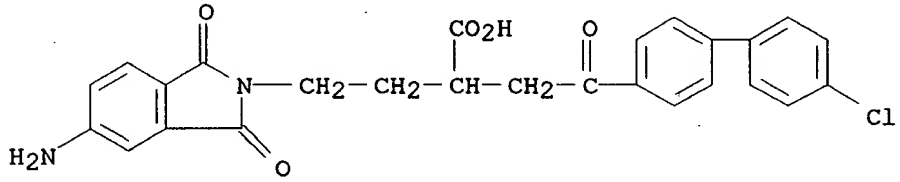
RN 179547-45-6 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo-5-propoxy- (9CI) (CA INDEX NAME)



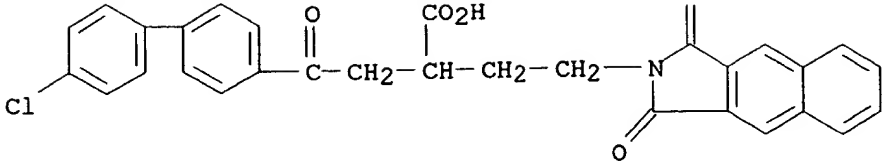
RN 179547-46-7 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3-dihydro-1,3-dioxo-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 179547-47-8 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
5-amino-.alpha.-[2-(4'-chloro[1,1'-biphenyl]-
4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

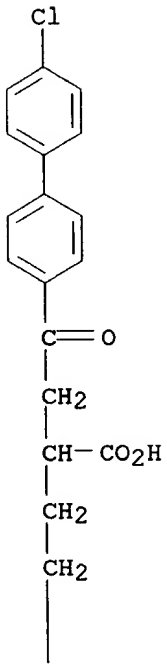


RN 179547-48-9 CAPLUS
CN 2H-Benz[f]isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-
4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

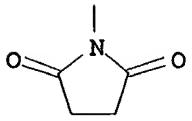


RN 179547-50-3 CAPLUS
CN 1-Pyrrolidinebutanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)

PAGE 1-A

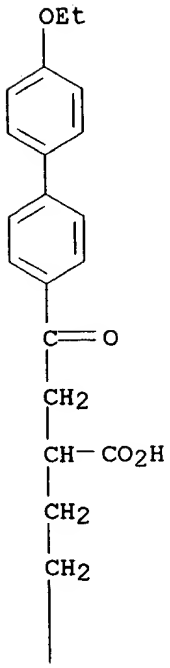


PAGE 2-A

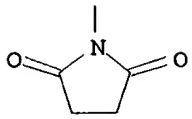


RN 179547-51-4 CAPLUS
CN 1-Pyrrolidinebutanoic acid, .alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)

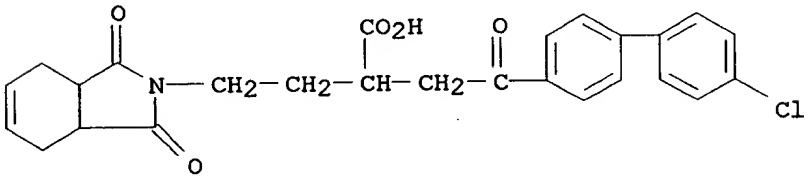
PAGE 1-A



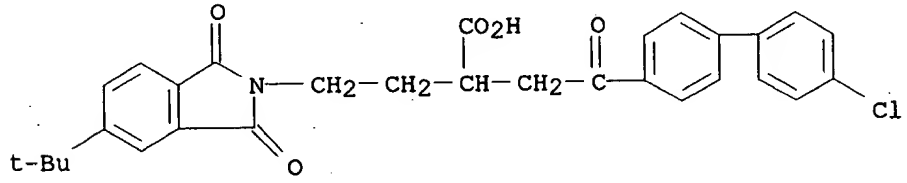
PAGE 2-A



RN 179547-52-5 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-1,3,3a,4,7,7a-hexahydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179547-53-6 CAPLUS
CN 2H-Isoindole-2-butanoic acid,
.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-
oxoethyl]-5-(1,1-dimethylethyl)-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179547-54-7 CAPLUS
CN 2H-Isoindole-2-butanoic acid, 5,6-dichloro-.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

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=> d l8 10-14 ibib abs hitstr

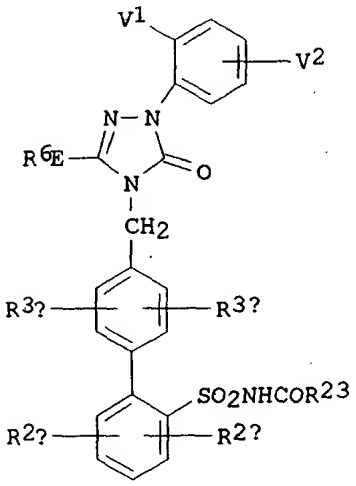
L8 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:607987 CAPLUS
DOCUMENT NUMBER: 123:286034
TITLE: Substituted triazolinones, triazolinethiones, and triazolinimines as angiotensin II antagonists
INVENTOR(S): Ashton, Wallace T.; Chang, Linda L.; MacCoss, Malcolm;
Chakravarty, Prasun K.; Greenlee, William J.; Patchett, Arthur A.; Flanagan, Kelly
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 90 pp. Cont.-in-part of U.S. Ser. No. 899,868, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5411980	A	19950502	US 1992-994228	19921221
ZA 9204916	A	19930331	ZA 1992-4916	19920702

PRIORITY APPLN. INFO.:

US 1989-386328	19890728
US 1990-504507	19900404
US 1991-725720	19910703
US 1991-812891	19911220
US 1992-899868	19921217

OTHER SOURCE(S): MARPAT 123:286034
GI



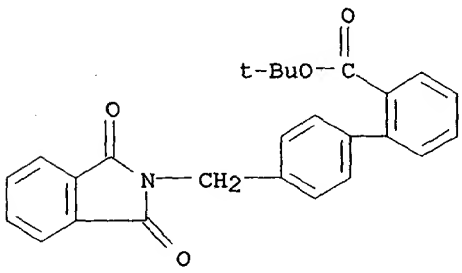
I

AB There are disclosed new substituted triazolinone compds. I [R2a = H, halo; R2b = H, halo, C1-4-alkyl; R3a = H, halo; R3b = H, halo, C1-4-alkyl; E is a single bond; R6 = (un)substituted C1-6-alkyl; R23 = e.g., (un)substituted Ph, branched C3-7-alkyl, C3-7-cycloalkyl; V1 = H, Me, CF3,

halogen, with the proviso that NR10R21; R10 = H, C1-4-alkyl; R21 = H or R22; R22 = e.g., C1-6-alkyl, C3-7-cycloalkyl; aryl] which are useful as angiotensin II antagonists. Thus, e.g., reaction of 4-bromomethyl-2'-(t-butoxycarbonyl)biphenyl with K phthalimide afforded 82% N-[[2'-(t-butoxycarbonyl)biphenyl-4-yl]methyl]phthalimide; hydrazinolysis afforded 88% 4-aminomethyl-2'-(t-butoxycarbonyl)biphenyl; reaction with CS2/MeI afforded 84% Me N-[[2'-(t-butoxycarbonyl)biphenyl-4-yl]methyl]dithiocarbamate; reaction of the latter with hydrazine afforded 79% 4-[[2'-(t-butoxycarbonyl)biphenyl-4-yl]methyl]-3-thiosemicarbazide; heterocyclization with tri-Me orthovalerate afforded 63% 4-[[2'-(t-butoxycarbonyl)biphenyl-4-yl]methyl]-5-butyl-2,4-dihydro-3H-1,2,4-triazole-3-thione; removal of the t-Bu group with trifluoroacetic acid afforded the corresponding 2'-carboxy deriv. (21%). Representative compds. of the invention act as angiotensin II receptor antagonists with activity of at least IC50 < 50 .mu.M. **Pharmaceutical** formulations were given.

IT **133690-72-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(substituted triazolinones, triazolinethiones, and triazolinimines as angiotensin II antagonists)

RN 133690-72-9 CAPLUS
CN [1,1'-Biphenyl]-2-carboxylic acid, 4'-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:470172 CAPLUS
DOCUMENT NUMBER: 122:239340
TITLE: Substituted amic acid derivatives useful for treatment of arteriosclerosis
INVENTOR(S): Nomoto, Takashi; Masahiro, Hayashi; Shibata, Jun; Iwasawa, Yoshikazu; Mitsuya, Morihiro; Iida, Yoshiaki; Nonshita, Katsumasa; Nagata, Yasufumi
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 94 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 611749	A1	19940824	EP 1994-102059	19940210
EP 611749	B1	19971022		

SE

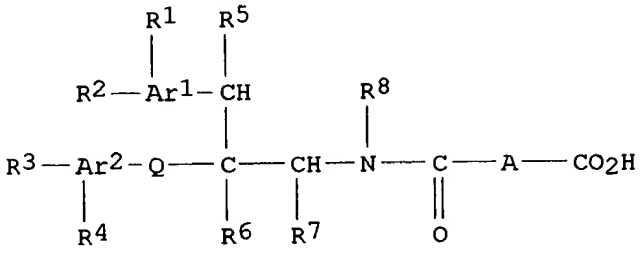
JP 07138214	A2	19950530	JP 1993-353833	19931228
AT 159514	E	19971115	AT 1994-102059	19940210
AU 9455046	A1	19940818	AU 1994-55046	19940211
US 5488149	A	19960130	US 1995-471081	19950606
US 5606101	A	19970225	US 1995-540329	19951006
US 5616803	A	19970401	US 1995-540628	19951006
US 5777150	A	19980707	US 1996-696152	19960813

PRIORITY APPLN. INFO.:

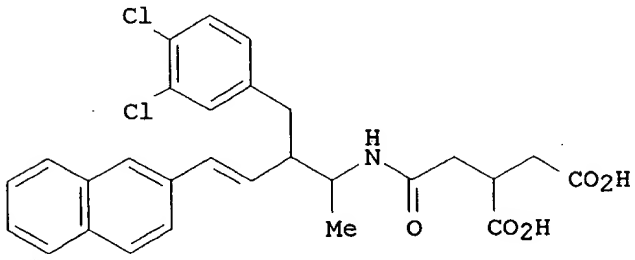
JP 1993-47364 19930212
JP 1993-261713 19930924
JP 1993-261714 19930924
US 1994-193850 19940209
US 1995-471081 19950606
US 1995-540329 19951006

OTHER SOURCE(S): MARPAT 122:239340

GI



I



III

AB Over 100 title compds. I [Ar1, Ar2 = (hetero)aryl nucleus; A = C3-8 linear (un)substituted (un)satd. aliph. hydrocarbon residue; Q = bond, CO2, OCO, CH2CH2, CH:CH, OCH2, SCH2, CH2O, CH2S; R1-R4 = H, halo, alkyl, OH, alkoxy, (un)substituted (hetero)aryl; R5-R7 = H, alkyl; R8 = H, alkyl, alkenyl, alkynyl, aralkyl; R1R2Ar1 and R3R4Ar2 .noteq. 4-ClC6H4 simultaneously when Q = bond] were prepd. I and their **pharmaceutically** acceptable salts and esters are inhibitors of squalene synthase, and are thus expected to be useful for treatment and/or prophylaxis of hypercholesterolemia, hyperlipemia, arteriosclerosis, and fungal infections. For example, tert-Bu 2-(3,4-dichlorobenzyl)acetoacetate was reduced by LiBH(Bu-sec)3 in THF at -70.degree. to give the (2RS,3RS) alc. (33%), which underwent further redn. to a 1,3-diol (90%), partial O-silylation (62%), Mitsunobu reaction of the unprotected secondary alc. with phthalimide (53%), desilylation (47%), oxidn. of the primary alc. to an aldehyde (73%), Wittig reaction with (2-naphthylmethyl)triphenylphospho nium chloride (75%), and hydrazinolysis of the imide (68%) to give the amine (1RS,2RS,3E)-2-(3,4-dichlorobenzyl)-1-methyl-4-(2-naphthyl)-3-

anhydride in THF in the presence of (iso-Pr)2NEt gave 58% amic acid (1RS,2RS,3E)-III. The IC50 of III for inhibition of human microsomal squalene synthase in vitro was 1.7 nM.

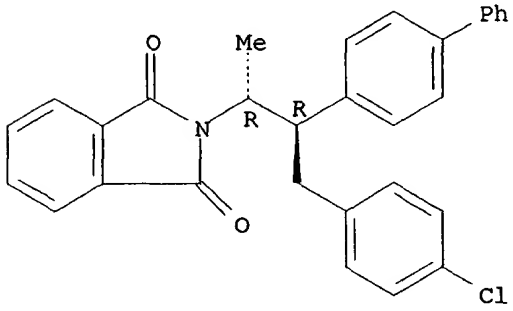
IT **162038-08-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. of substituted amic acid derivs. as squalene synthase inhibitors)

RN 162038-08-6 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[1,1'-biphenyl]-4-yl-3-(4-chlorophenyl)-1-methylpropyl]-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L8 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:477643 CAPLUS

DOCUMENT NUMBER: 111:77643

TITLE: Preparation of new phenylethanolamines and **pharmaceuticals** containing them

INVENTOR(S): Hurnaus, Rudolf; Reiffen, Manfred; Sauter, Robert; Grell, Wolfgang; Rupprecht, Eckhard

PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Fed. Rep. Ger.

SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3718638	A1	19881222	DE 1987-3718638	19870604
WO 9006299	A1	19900614	WO 1988-EP1083	19881129
W: AU, DK, JP, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8826115	A1	19900626	AU 1988-26115	19881129
AU 617139	B2	19911121		
EP 375791	A1	19900704	EP 1988-119850	19881129
R: ES, GR				
EP 400011	A1	19901205	EP 1989-900024	19881129
EP 400011	B1	19940126		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03503405	T2	19910801	JP 1989-500051	19881129
AT 100792	E	19940215	AT 1989-900024	19881129
CA 1325210	A1	19931214	CA 1988-584935	19881202
DK 9001619	A	19900705	DK 1990-1619	19900705
US 5232946	A	19930803	US 1990-572969	19900820

PRIORITY APPLN. INFO.:

DE 1987-3718638	19870604
EP 1989-900024	19881129
WO 1988-EP1083	19881129

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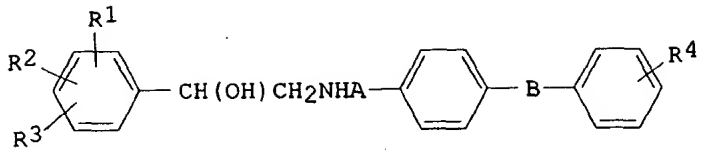
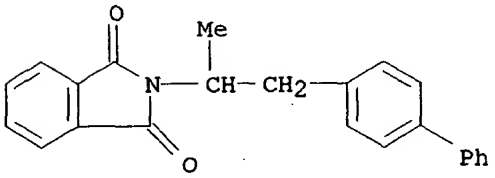


I

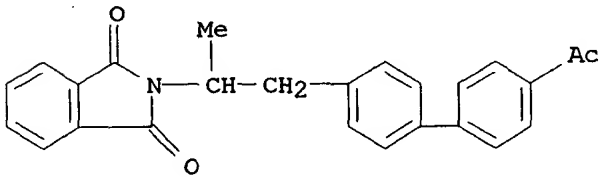
AB The title compds. [I; A = C1-5 alkylene; B = bond, C1-2 alkylene, CO, CHOH; R1 = H, halo, CF3; R2 = H, NH2; R3 = H, cyano, Cl, Br; R4 = H, halo, alkyl, OH, (un)substituted alkoxy, etc.], their optical isomers, diastereomers, and salts, useful in treatment of diabetes mellitus, obesity, and for treatment and prophylaxis of atherosclerosis, were prepd. by 7 methods. 4-PhC6H4CO2Et in CH2Cl2 was treated with AlCl3 and MeCHClCOCl in CH2Cl2 at 0.degree. and kept overnight at room temp. to give 4-(4-MeCHClCOC6H4)C6H4CO2Et which was refluxed 2 days with KOAc in Me2CO to give 4-[4-AcOCHMeCOC6H4]C6H4CO2Et. NaBH4 redn. and heating with polyphosphoric acid at 80.degree. gave 4-(4-MeCOCH2C6H4)C6H4CO2Et which was treated with 3-ClC6H4CH(OH)CH2NH2 in EtOH contg. NaBH3CN and AcOH at room temp. to give I (R1 = 3-Cl, R2 = R3 = H, A = CHMeCH2, B = bond, R4 = 4-CO2Et) (II). In mice 1 and 3 mg II/kg orally decreased blood sugar 37% and 49%, resp., vs. a control. A formulation for dragees comprised I (R1 = 3-Cl, R2 = R3 = H, A = CHMeCH2, B = CH2, R4 = 2-CO2Et) 10.0, lactose 69.0, corn starch 35.0, polyvinylpyrrolidone 5.0, and Mg stearate 1.0 mg.

IT **121804-25-9P 121804-26-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in synthesis of **pharmaceutical** phenylethanolamine deriv.)

RN 121804-25-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(2-[1,1'-biphenyl]-4-yl-1-methylethyl)-(9CI) (CA INDEX NAME)



RN 121804-26-0 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4'-acetyl[1,1'-biphenyl]-4-yl)-1-methylethyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2001 ACS

DOCUMENT NUMBER: 104:88265
TITLE: (2-, 3- And 4-Biphenylyloxy)aminoalkanes and related compounds and their uses
INVENTOR(S): Nelson, Peter H.; Unger, Stefan H.; Dunn, James P.; Thieme, Thomas R.
PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA
SOURCE: Eur. Pat. Appl., 73 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 157652	A1	19851009	EP 1985-302406	19850404
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4792570	A	19881220	US 1984-597790	19840406
JP 60231634	A2	19851118	JP 1985-73385	19850405
ES 550876	A1	19870701	ES 1986-550876	19860114
PRIORITY APPLN. INFO.:			US 1984-597282	19840406
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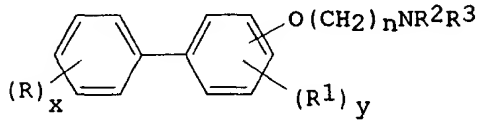
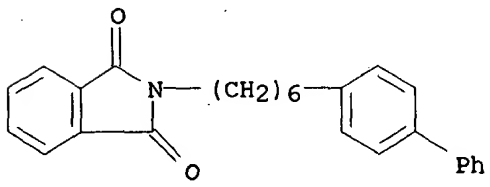


I

AB Title compds. I [R, R1 = H, alkyl, halo, alkoxy, cycloalkyl, Ph; R2 = H, alkyl, cycloalkyl; R3 = H, alkyl, cycloalkyl, CH2CH2OH; R2R3 = (CH2)3-8, NR2R3 = morpholino, 1-piperazinyl with optional alkyl or hydroxyethyl substituent; n = 3-12; x = 0-3; y = 0-2], useful for treating inflammation, swelling and assocd. pain, and psoriasis, were prepd. Thus, Cl(CH2)6OH was tosylated and the tosylate was treated with 2-PhC6H4OH to give 2-PhC6H4O(CH2)6Cl (II). II was treated with K phthalimide to give the phthalimido deriv. which was treated with N2H4.H2O to give 2-PhC6H4O(CH2)6NH2 (III). II was aminated with Me2NH to give 2-PhC6H4O(CH2)6NMe2 (IV). IV inhibited inflammation by 33% in the croton oil-inflamed rat ear assay and cleared psoriatic lesions in 60% of cases tested by method of K. J. Dumas et al. (1972). Tablets (200 mg) were prepd. contg. III 25, corn starch 20, spray-dried lactose 153, and Mg stearate 2 mg.

IT **100444-47-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrazinolysis of)

RN 100444-47-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(6-[1,1'-biphenyl]-4-ylhexyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 14 OF 14 CAPLUS

ACCESSION NUMBER: 1982:457122 CAPLUS
DOCUMENT NUMBER: 97:57122
TITLE: Biphenyl compounds and their use as intermediates in optical brighteners, dyes, plastics and **pharmaceutical** preparations
INVENTOR(S): Harnisch, Horst
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 50 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 47877	A2	19820324	EP 1981-106467	19810820
EP 47877	A3	19820602		
EP 47877	B1	19850123		
R: CH, DE, FR, GB, IT				
DE 3048088	A1	19820715	DE 1980-3048088	19801219
US 4370486	A	19830125	US 1981-292868	19810814
JP 57077630	A2	19820515	JP 1981-135645	19810831
JP 02054334	B4	19901121		

PRIORITY APPLN. INFO.: DE 1980-3033002 19800902
DE 1980-3048088 19801219

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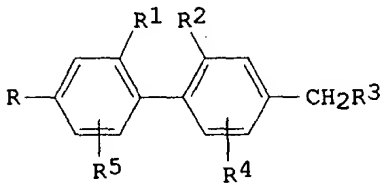
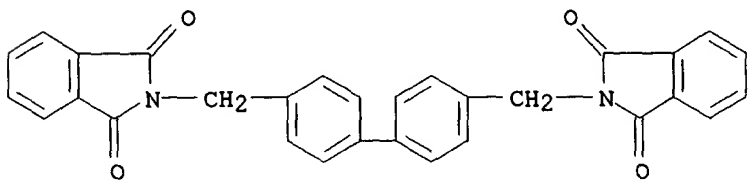


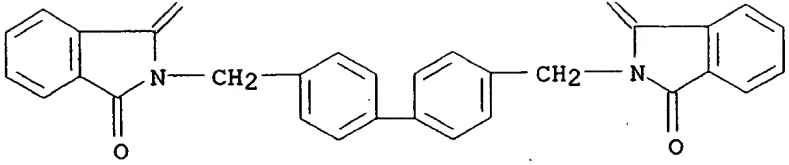
I

AB Title compds. (I; R = H, CH2R3, SO3H, C1-6 alkyl, CF3, cyclohexyl, C1-4 alkoxy, Cl, Br, F; R1 = H, Me; R2 = H, RR1 = CH2CH2, SO2; R3 = halogen .alpha.-substituted acetamido, propionamide, optionally substituted benzamido, phthalimido; R4 = H, Me, SO3H; R5 = H, Me, Cl, SO3H; with the proviso R3 = halogen substituted acetoamido or propionamido or optionally substituted benzamido when no SO3H groups or SO2 bridges are present) are prepd. Thus, biphenyl [92-52-4] in propionic acid contg. H2SO4 was reacted with chloroacetamide [79-07-2] and paraformaldehyde [30525-89-4]
to give I (R = ClCH2CONHCH2; R1 = R2 = R4 = R5 = H; R3 = ClCH2CONH) [82487-54-5]. Approx. 30 other I were prepd.

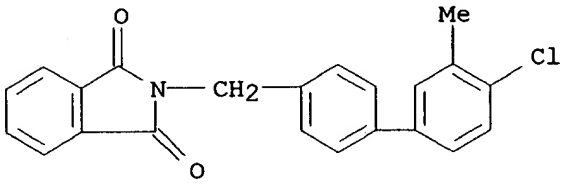
IT **82487-22-7P 82487-30-7P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(prepn. of)

RN 82487-22-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2,2'-[[1,1'-biphenyl]-4,4'-diylbis(methylene)]bis- (9CI) (CA INDEX NAME)





RN 82487-30-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[(4'-chloro-3'-methyl[1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	88.97	222.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.17	-11.17

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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L9 2 L3

=> d l9 1-2 ibib abs hitstr

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BIB ----- AN, TI, AU, PA, DT, PI
CAN ----- List of CA abstract numbers, no L-number headers

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IND ----- Indexing data
MAX ----- Same as ALL
SAM ----- TI, IT
SCAN ---- TI, IT (random display, no answer numbers;
SCAN must be entered on the same line as the DISPLAY,
e.g., D SCAN or DISPLAY SCAN)
STD ----- BIB

IALL ---- ALL, indented with text labels
IBIB ---- BIB, indented with text labels
ISTD ---- STD, indented with text labels

HIT ----- Fields containing hit terms
HITIND -- IT
HITRN --- HIT RN
HITSTR -- HIT RN, its CA index name and its structure diagram
FHITSTR - First HIT RN, its CA index name and its structure diagram
OCC ----- Number of occurrence of hit term and fie ld in which it occurs

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Numbers (AN) CA References.

Index Terms in CAOLD include only Registry Numbers; no
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PAGE ---- Page Image of original Chemical Abstracts issue containing the
abstract of the answer.
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the current answer.
ENTER DISPLAY FORMAT (ALL):all

L9 ANSWER 1 OF 2 CAOLD COPYRIGHT 2001 ACS
AN CA62:8968b CAOLD
TI mechanism of the Gabriel-Colman rearrangement
AU Hill, John H. M.
IT 794-43-4 796-40-7 798-63-0 897-23-4 897-24-5 907-49-3
970-56-9 973-11-5 **980-09-6** 1032-67-3 1039-78-7
1909-25-7

L9 ANSWER 2 OF 2 CAOLD COPYRIGHT 2001 ACS
AN CA54:24473g CAOLD
TI aminomethylation of aromatic compds.
AU Gornostaeva, S. E.; Kornev, K. A.
IT 539-48-0 2457-28-5 3145-43-5 3145-44-6 4934-35-4 17564-64-6
30391-55-0 31912-78-4 33891-01-9 **82487-22-7** 97705-28-7
102876-36-8 103158-37-8 109937-36-2 111442-77-4 113135-69-6 118873-55-5
119339-42-3 121622-79-5 122446-56-4 122725-28-4

=>

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.39	224.07

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-11.17

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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Dec 17  The CA Lexicon available in the CAPLUS and CA files
 NEWS  3  Feb 06  Engineering Information Encompass files have new names
 NEWS  4  Feb 16  TOXLINE no longer being updated
 NEWS  5  Apr 23  Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23  PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
 NEWS  7  May 07  DGENE Reload
 NEWS  8  Jun 20  Published patent applications (A1) are now in USPATFULL

 NEWS EXPRESS  May 23 CURRENT WINDOWS VERSION IS V6.0a,
               CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP),
               AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001
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DICTIONARY FILE UPDATES:  20 JUN 2001  HIGHEST RN 342773-47-1

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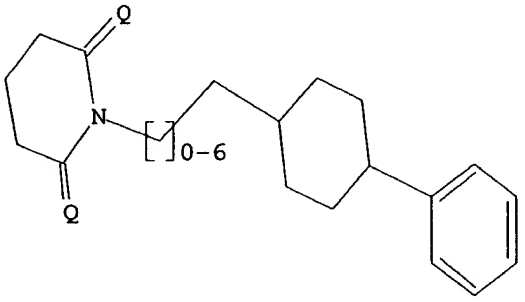

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SAMPLE SEARCH INITIATED 16:48:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2532 TO ITERATE

39.5% PROCESSED 1000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 47624 TO 53656
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

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100.0% PROCESSED 48719 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.06

L3 2 SEA SSS FUL L1

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	133.87	134.32

FILE 'CAPLUS' ENTERED AT 16:49:17 ON 21 JUN 2001

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FILE COVERS 1947 - 21 Jun 2001 VOL 134 ISS 26
FILE LAST UPDATED: 20 Jun 2001 (20010620/ED)

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L4 2 L3

=> d l4 1-2 ibib abs hitstr

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:534889 CAPLUS
DOCUMENT NUMBER: 129:161412
TITLE: Derivatives of substituted 4-biarylbutyric acid as matrix metalloprotease inhibitors
INVENTOR(S): Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt, Michael Christopher; Wolanin, Donald John; Wilhelm, Scott M.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S., 109 pp. Cont.-in-part of U.S. Ser. No. 339,846.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5789434	A	19980804	US 1995-539409	19951106
CA 2201863	AA	19960523	CA 1995-2201863	19951109

HU 78083	A2	19990830	HU 1998-233		19951109
US 5874473	A	19990223	US 1997-864666		19970528
US 5886024	A	19990323	US 1997-865325		19970528
US 5854277	A	19981229	US 1997-865639		19970530
US 5859047	A	19990112	US 1997-866798		19970530
US 5861427	A	19990119	US 1997-866679		19970530
US 5861428	A	19990119	US 1997-866680		19970530
US 5886043	A	19990323	US 1997-866778		19970530
US 6166082	A	20001226	US 1998-57679		19980409

PRIORITY APPLN. INFO.:

US 1994-339846	A2	19941115
US 1995-462729	B1	19950605
US 1995-463490	B1	19950605
US 1995-463580	B1	19950605
US 1995-463794	B1	19950605
US 1995-464253	B1	19950605
US 1995-465626	B1	19950605
US 1995-539409	A1	19951106

OTHER SOURCE(S): MARPAT 129:161412

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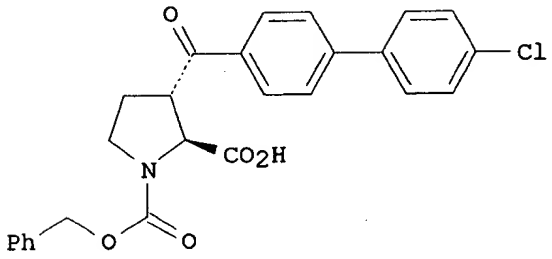


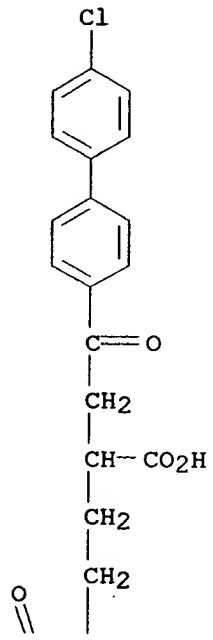
I

AB Matrix metalloprotease (MMP) inhibitors TxA-B-D-E-G [I; T = halo, haloalkyl, alkynyl, (un)substituted alkyl or alkenyl; x = 0, 1, 2; A, B = arom. or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, 5-tetrazolyl, etc.] and their pharmaceutically acceptable salts were prepd. In particular, I [A = C6H4; B = 1,4-C6H4; E = certain substituted THF, tetrahydrothiophene, or pyrrolidine divalent radicals] with MMP inhibitory activity, and their pharmaceutically acceptable salts, are claimed. For instance, claimed title compd. II was prepd. from L-pyroglutaminol in 9 steps. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. For instance, II had corresponding IC50 values of 103, 381, and 35 nM. I inhibited tumor growth and metastasis in animal models, and inhibited cartilage lesions in a guinea pig model of osteoarthritis.

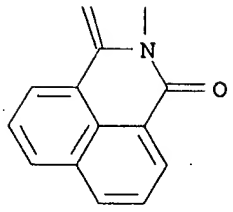
IT **179547-49-0P 179547-57-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179547-49-0 CAPLUS

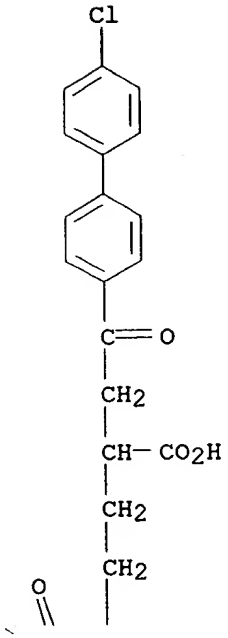
CN 1H-Benz[de]isoquinoline-2(3H)-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)

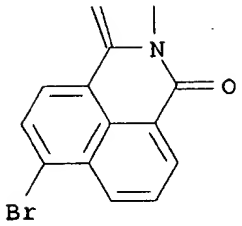


PAGE 2-A



RN 179547-57-0 CAPLUS
CN 1H-Benz[de]isoquinoline-2(3H)-butanoic acid, 6-bromo-.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)





L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:476807 CAPLUS
DOCUMENT NUMBER: 125:142275
TITLE: Substituted 4-biarylbutyric or 5-biarylpentanoic acids and derivatives as matrix metalloprotease inhibitors
INVENTOR(S): Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt, Michael Christopher; et al.
PATENT ASSIGNEE(S): Bayer A.-G., USA
SOURCE: PCT Int. Appl., 263 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615096	A1	19960523	WO 1995-US14002	19951109

GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2201863	AA	19960523	CA 1995-2201863	19951109
AU 9641975	A1	19960606	AU 1996-41975	19951109
AU 702317	B2	19990218		
EP 790974	A1	19970827	EP 1995-940572	19951109

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

BR 9509686	A	19970930	BR 1995-9686	19951109
CN 1163604	A	19971029	CN 1995-196209	19951109
JP 10509146	T2	19980908	JP 1995-516097	19951109
HU 78083	A2	19990830	HU 1998-233	19951109
FI 9702062	A	19970714	FI 1997-2062	19970514
NO 9702220	A	19970714	NO 1997-2220	19970514
US 5874473	A	19990223	US 1997-864666	19970528
US 5886024	A	19990323	US 1997-865325	19970528
US 5854277	A	19981229	US 1997-865639	19970530
US 5859047	A	19990112	US 1997-866798	19970530
US 5861427	A	19990119	US 1997-866679	19970530
US 5861428	A	19990119	US 1997-866680	19970530
US 5886043	A	19990323	US 1997-866778	19970530

PRIORITY APPLN. INFO.:	US 1994-339846	A	19941115
	US 1995-462729	B1	19950605
	US 1995-463490	B1	19950605
	US 1995-463580	B1	19950605
	US 1995-463794	B1	19950605
	US 1995-464253	B1	19950605
	US 1995-465626	B1	19950605
	WO 1995-US14002	W	19951109

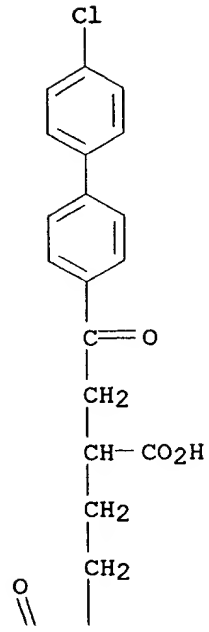
OTHER SOURCE(S): MARPAT 125:142275

AB Matrix metalloprotease inhibitors TxA-B-D-E-G [Tx = substituent such as halo, C1-C10 alkyl, or cyanoalkenyl; x = 0, 1, 2; A, B = arom. or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, etc.] and their pharmaceutically acceptable salts were prepd. Thus, (S)-.gamma.-oxo-4'-(pentyloxy)-.alpha.-(3-phenylpropyl)-[1,1'-biphenyl]-4-butanoic acid (86) was prepd. via alkylation of di-Et (3-phenylpropyl)malonate with 2,4'-dibromoacetophenone, followed by sapon.-monodecarboxylation, reaction with 4-methoxybenzeneboronic acid, Me ether cleavage, and O-pentylation. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. Using compds. such as 86, the no. of tumor metastases was decreased between 38 and 49% as compared to the control. The title compds. were also assayed for inhibition of cartilage lesions in a guinea pig model of osteoarthritis.

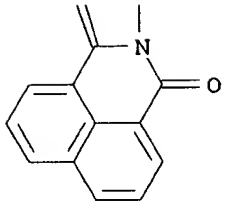
IT **179547-49-0P 179547-57-0P**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179547-49-0 CAPLUS

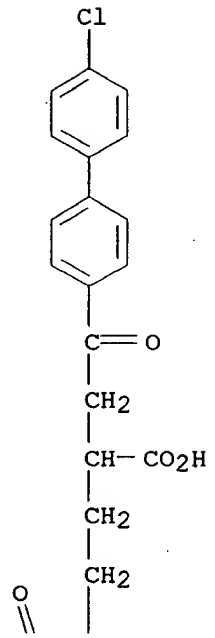
CN 1H-Benz[de]isoquinoline-2(3H)-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)

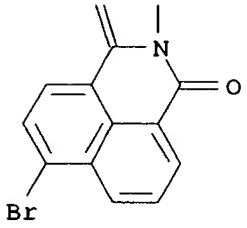


PAGE 2-A



RN 179547-57-0 CAPLUS
CN 1H-Benz[de]isoquinoline-2(3H)-butanoic acid, 6-bromo-.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)





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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.18	-1.18

STN INTERNATIONAL LOGOFF AT 16:49:52 ON 21 JUN 2001